

## PATENT COOPERATION TREATY

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## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ISPH-0590WO	<b>FOR FURTHER ACTION</b> <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/US04/18932	International filing date (day/month/year) 15 July 2004 (15.07.2004)	(Earliest) Priority Date (day/month/year) 15 July 2003 (15.07.2003)
Applicant ISIS PHARMACEUTICALS INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the Report

a. With regard to the language, the international search was carried out on the basis of:

☒  
☐

the international application in the language in which it was filed.

a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☒

With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐

Certain claims were found unsearchable (See Box No. II)

3. ☒

Unity of invention is lacking (See Box No. III)

4. ☐

With regard to the title,

☒  
☐

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

## 5. With regard to the abstract,

☒  
☐

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

## 6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_

☐  
☐  
☐

as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

b. ☒

none of the figures is to be published with the abstract.

Form PCT/ISA/210 (first sheet) (April 2005)

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/18932

## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item I.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

## a. type of material



a sequence listing



table(s) related to the sequence listing

## b. format of material



on paper



in electronic form

## c. time of filing/furnishing



contained in the international application as filed



filed together with the international application in electronic form



furnished subsequently to this Authority for the purposes of search

2. ☒

In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

Form PCT/ISA/210 (continuation of first sheet(1)) (April 2005)

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/18932

**Box No. II** Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III** Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-27, 29, 45-55 and SEQ ID NO: 94

- Remark on Protest
- |                          |                                                                                                                                                                       |
|--------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input type="checkbox"/> | The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.                                           |
| <input type="checkbox"/> | The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation. |
| <input type="checkbox"/> | No protest accompanied the payment of additional search fees.                                                                                                         |

Form PCT/ISA/210 (continuation of first sheet(2)) (April 2005)

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/18932

## A. CLASSIFICATION OF SUBJECT MATTER

IPC: C07H 21/04 (2006.01); A61K 31/70 (2006.01)

USPC: 536/24.5; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 536/24.5; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
EAST, STN: stearyl CoA desaturase, antisense, STIC search of SEQ ID NO: 94

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 20030083282 A1 (CROOKE et al.) 1 May 2003 (01.05.2003), see entire document	1-27, 29 and 46-55

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

\* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"Z" document member of the same patent family

Date of the actual completion of the international search  
21 March 2006 (21.03.2006)Date of mailing of the international search report  
17 APR 2006Name and mailing address of the ISA/US  
Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
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Form PCT/ISA/210 (second sheet) (April 2005)

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US04/18932**BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Groups 1-292, claim(s) 1 in part, 2-27, 29 and 46-55, drawn to a compound 8-50 nucleotides in length targeted to a nucleic acid molecule encoding stearoyl-CoA desaturase comprising a sequence selected from the 292 sequences recited in claim 1.

Group 293, claim(s) 28, 30-32 and 35-45, drawn to a method of inhibiting expression of stearoyl-CoA desaturase using a compound at least 80% complementary to at least 8 nucleobases of a nucleic acid encoding stearoyl-CoA desaturase.

Group 294, claim(s) 33 and 34, drawn to use of the compound of claim 1 in preparation of a medicament for treatment of a disease associated with stearoyl-CoA desaturase.

The inventions listed as Groups 1-294 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of inventions 1-292 is a compound 80% complementary to at least 8 nucleobases of any of the sequences shown in claim 1. Such compounds were known in the art prior to the time of invention. See for example US 20030083282 A1, which discloses antisense oligonucleotides directed to stearoyl CoA desaturase. One of these oligonucleotides, SEQ ID NO: 65, shares 7 nucleotides in common with instant SEQ ID NO: 99, making this sequence 80% complementary to an 8 nucleobase fragment of SEQ ID NO: 99.

Further, according to the guidelines in Section (f)(7)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the claimed polynucleotide sequences, the Markush group shall be regarded as being of similar nature when:

(A) all alternatives have a common property or activity and

(B)(1) a common structure is present, i.e., a significant structure is shared by all of the alternatives or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant antisense sequences are considered to be each separate inventions for the following reasons:

The sequences do not meet the criteria of (A), common property or activity or (B)(2), art recognized class of compounds. Although the antisense sequences of the instant application all target and modulate expression of the same gene, each antisense sequence behaves in a different way in the context of the claimed invention. Each sequence targets a different and specific region of stearoyl CoA desaturase and each sequence modifies (either increases or decreases) the expression of the gene to varying degrees (as shown in Table 1). Each member of the class cannot be substituted; one for the other, with the expectation that the same intended result would be achieved.

Further, although the instant antisense sequences target the same gene, the sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the antisense sequences of the instant application is lacking and each antisense sequence claimed is considered to constitute a special technical feature.

Form PCT/ISA/210 (extra sheet) (April 2005)